Normal range of N-terminal pro-brain natriuretic peptide: a note of caution

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DOI: https://doi.org/10.1093/eurheartj/ehi738

the former. My editorial highlighted the latter. Cardioversions are often done within 7 days or even 24 h from the onset of AF. Some of these episodes of AF will indeed be long-lasting (persistent AF) but some would be short-term and would self-terminate if allowed to do so (paroxysmal AF). The Guidelines committee recognized the problem and chose a pragmatic but arbitrary approach, calling for all of these to be classified as episodes of persistent AF.[1] The AF Guidelines are currently being re-written but the classification scheme is unaltered. Any modifications to the current scheme should be simple, practical, and evidence-based, if possible. To modify the scheme a wide consensus should be sought and the imprimatur of professional organizations, such as the European Cardiac Society, American Heart Association, American College of Cardiology, Heart Rhythm Society, and others would be highly desirable.

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doi:10.1093/eurheartj/ehi738

Online publish-ahead-of-print 23 January 2006

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With interest we read the article by Galasko *et al*.[1] in a recent issue. The authors present age- and gender-stratified normal values for N-terminal pro-brain natriuretic peptide (NTpBNP), which they validated in subjects with high risk for cardiovascular disease recruited from community practices and in a random sample of low-risk subjects without cardiovascular risk factors. In this study, the definition of significant cardiovascular disease was based on a history of cardiovascular risk factors and coronary artery disease (CAD) as well as pathologic echocardiographic findings. However, the authors' conclusion that the cut-off values provided offer excellent negative and positive predictive values for ruling in or out cardiovascular disease should be taken with caution. Significant cardiovascular disease cannot be ruled out by these cut-off values, because Galasko *et al*. did not reliably rule out silent CAD in the subjects assessed. Especially for groups with higher prevalence of CAD, as in older subjects, or with a higher rate of silent CAD, as in women, the cut-off values given might be too high. NTpBNP has been shown to be elevated in patients with CAD,[2] and elevated levels are associated with adverse outcomes.[3] Unless CAD is not excluded by an accurate diagnostic reference method, i.e. coronary angiography, subjects with silent but significant CAD will be misclassified as free of significant cardiovascular disease. In the paper addressed, NTpBNP levels of subjects with silent CAD might have been included in the calculation of the upper limit of the normal range of NTpBNP. The upper limit of the normal range of NTpBNP might therefore be lower than that stated in the study of Galasko *et al*.

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doi:10.1093/eurheartj/ehi739

Online publish-ahead-of-print 23 January 2006

Normal range of N-terminal pro-brain natriuretic peptide: a note of caution: reply

We would like to answer to Wolber and Maeder's comments in turn.

They state that our conclusions must be taken with caution, as silent coronary artery disease (CAD) was not ruled out. There is, however, no evidence that screening for silent CAD even by coronary angiography produces prognostic benefit, so we were entitled not to assess this, sticking to conditions where early screening may be beneficial. Moreover, our conclusions stated that normal NTpBNP levels ruled out many significant cardiovascular conditions, not cardiovascular disease in general as they suggest.

They are similarly concerned that the developed NTpBNP upper reference values may be too high as subjects with silent CAD could have been included in the normal group, recommending diagnostic angiography in these subjects. Certainly, we tried to make this group as normal as possible, excluding